**Remarks**

In view of the foregoing amendments and the following remarks, reconsideration of the present patent application is respectfully requested.

**Rejection under 35 U.S.C. 112, first paragraph:**

Applicants have amended claim 1 to correct typographical errors both in the scheme and the drawings.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for methods of preparing polypyrrolinones, the specification does not reasonably provide enablement for a method using any base for cyclization of an imine and any base for oxidation of a primary alcohol to an aldehyde. Applicants respectfully traverse

Applicant's invention evidenced by Applicant's Specification and Examples therein is directed to reacting an aldehyde comprising portion of an alpha-amino-alpha-substituted-1,4-dioxo compound (as cited in claim 1 and throughout the specification) with a 2-substituted-2-aminovalerolactone and trimethylorthoformate to produce the imine.

Second, the imine is treated with a base to form a metalloimine carbanion, optionally in the presence of a crown ether that forms a pyrrolinone through intra molecular cyclization.

Lastly, the primary alcohol is oxidized to an aldehyde which allows the above-described synthesis to be repeated generating polypyrrolinone.

The Examiner alleges that the above process is too broad because the reagents for these steps are not "specifically" specified.

Further, the Examiner alleges that the prior art teaches that bases other than KHMDS used for cyclization of claim 1 "do not work" (e.g., see Smith, A.B.; Liu, H.; Hirschman, R. "A Second-Generation Synthesis of Polypyrrolinone Nonpeptidomietics

Prelude to the Synthesis of Polypyrrolinones on Solid Support" Organic Letters 2000, 2, 14, 2037-3040, page 2039, paragraph 2. Applicants respectfully traverse.

Applicants wish to point out to the Examiner that the cited reference does not teach that bases other than KHMDS used for cyclization of claim 1 "do not work".

The reference states that "other amide basis, such as LDA, LTMP, and LiHMDS, led to unsaturated lactam (-)-20 as a major side product (ca. 40%)." These amide bases work they however have not reduced the formation of the undesired unsaturated lactam (-)-20 as a major side product as compared to when KHMDS/18-crown is employed (lactam (-)-20 was formed in less than 5%).

The Examiner further contends that a wide variation in product yield even for bases that are almost identical clearly demonstrates the "unpredictable" nature of the cyclization reaction and/or its inherent limitations.

Applicants stress that other amide bases, such as LDA, LTMP, and LiHMDS can be utilized for the cyclization step and in fact would be employed by those skilled in the art. Variations of similar amide bases do cause differences in the yield of generating desired products, as does technique used in adding the amide base to the reaction used by the experimenter. However, because one amide base generates a better yield than another amide base does not preclude patentability. An invention must be "useful", not "more useful" or "most useful". 35 U.S.C. 101. Therefore in lieu of KHMDS, other amide bases, such as LDA, LTMP, and LiHMDS are useful.

The Examiner similarly alleges, "the prior art also teaches that mild oxidation reagents in a Swern oxidation must be used" (p.6 of Communication paper No. 10). Further, the Examiner alleges that other reagents led to decomposition and that stronger reagents like powerful transition metal oxidants would almost certainly destroy these compounds.

Applicants wish to direct the Examiner to page 13 of Applicant's specification. Page 13 of Applicant's specification clearly teaches and enables those skilled in the art which oxidizing reagents to utilize in practicing the invention.

The Examiner also alleges that the inventor provides no guidance beyond the aforementioned Examples taught in the specification. As a result, one of ordinary skill in the art could not predict what other types of compounds could effectively be synthesized via methods of the claimed invention and, consequently, an indeterminate quantity of experimentations would be necessary to synthesize "all" possible compounds as a "high load" Merrifield Resin.

Further, the Examiner cites language from *In re Vaeck,* 947 F.2d 488, 496 indicating "There must be sufficient disclosure, either through illustrative examples or technology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed". Applicants traverse.

As stated above concerning the issue of amide bases and oxidizing reagents applicants' disclosure enables those skilled in the art to practice Applicant's invention.

Furthermore, the specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Boskowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Also, "the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F.2d 731, 737, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

Accordingly, Applicants need not provide Examples of every species claimed in Applicants' patent application. Applicants' specification enables those skilled in the art

to react an aldehyde comprising portion of an alpha-amino-alpha-substituted-1,4-dioxo compound with a 2-substituted-2-amino valerolactone and trimethylorthoformate to produce an imine. Treat the imine with a base to form a metalloimine carbanion, optionally in the presence of a crown ether to form a pyrrolinone and oxidize a primary alcohol to an aldehyde, allowing the above-described synthesis to be repeated. Further to the holding in *In re Wands*, those skilled in the art routinely substitute the above-mentioned amide bases based on the reactive properties of the substituents associated with the molecules being used. The various substitutions of the amide bases is a routine experimental process used by those skilled in the art and not undue experimentation.

Based on the foregoing Applicants respectfully request that the 35 U.S.C. 112, first paragraph with respect to claims 1-7 be withdrawn.

**Rejection under 35 U.S.C. 112, second paragraph:**

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Below are the particulars for specific claims rejected under 35 U.S.C. 112, second paragraph, cited by Examiner.

A. Claims 1 and 3 are rejected because the term "lower" as used in conjunction with "alkyl" or "alkoxy", etc. is vague and indefinite. Applicants have amended claims 1 and 3 to remove the term "lower" and replace it with $C_1$-$C_8$. Support for the amendment can be found on page 6 and page 7 of Applicants specification as originally filed.

B. Claim 1 recites an improper Markush format. Applicants have amended claim 1 to include a proper Markush format.

C. Claim 1 is rejected because the term "exposing" as used in the cited method step is vague and indefinite. Applicants have amended claim 1 to remove the term "exposing" and replace it with the term "reacting".

D. Claim 1 is rejected because the phrase "plurality of treatments" is vague and indefinite. Applicants have amended claim 1 to remove the phrase "plurality of treatments".

E. Claim 2 is rejected because claim 2 recites "substantially" diastereomerically pure in line 1. The Examiner alleges that "substantially" is a relative term, which renders the claim indefinite and/or unclear. Applicants traverse.

It is well understood by those skilled in the art that it is nearly impossible to isolate a diastereomerically pure isomer (that is, no trace of the other diastereomer). Those skilled in the art generally conclude that a compound is substantially pure if it contains <10% of undesired elements.

Further, in *Andres Corp. v. Gabriel Electronics*, 847 F.2d 819, 6 USPQ 2d 2010 (Fed. Cir. 1988) the court held that the limitation "which produces substantially equal E and H plane illumination patterns," was definite because one of ordinary skill in the art would know what was meant by "substantially equal".

Here, as discussed above, one skilled in the art would know what was meant by "substantially pure" particularly with respect to chemical compounds.

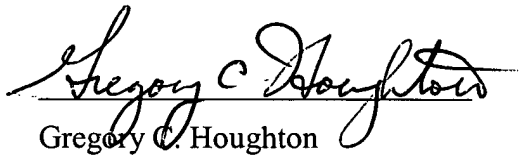
Based on the foregoing, Applicants respectfully request that the 35 U.S.C. 112, second paragraph, rejection with respect to claims 1-7 be withdrawn.

## Conclusion

In view of the remarks and the amendments, further and favorable consideration of the present application and the allowance of all pending claims are respectfully requested. The Examiner is also invited to contact the undersigned should the Examiner believe that such contact would expedite prosecution of the present application.

It is believed that no fee is required in connection with the filing of the present Amendment. However, if any fee is required, the Commissioner is authorized to charge any such fees or credit any overpayment to Deposit Account No. 13-2165.

Respectfully submitted,



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